

Applicants: Collin J. Weber et al.  
Serial No.: 09/049,865  
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#### **REMARKS**

Claims 54-59 and 62-70 are pending in the subject application. By this Amendment, claims 54-59 and 62-69 have been canceled without prejudice or disclaimer. Applicants herein add new claims 71-81. Support for amended claim 70 can be found in the specification, inter alia, on page 28, lines 3-6 and page 62, lines 9-11. Support for new claims 71-73 can be found in the specification, inter alia, on page 41, lines 3-6. Support for new claims 74 and 75 can be found in the specification, inter alia, on page 32, lines 15-26. Support for new claim 76 can be found in the specification, inter alia, on page 32, line 10. Support for new claims 77 and 78 can be found in the specification, inter alia, on page 32, lines 2-4. Support for new claim 79 can be found in the specification, inter alia, on page 32, lines 28-30. Support for new claims 80 and 81 can be found in the specification, inter alia, on page 33, lines 15-19. Applicants maintain that this Amendment raises no issue of new matter. Accordingly, upon entry of this Amendment, claims 70-81 will be pending and under examination.

In view of the arguments set forth below, applicants maintain that the Examiner's objection and rejections made in the December 16, 2004 Final Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

#### **The Claimed Invention**

This invention provides a method for transplanting into a subject a viable xenogeneic cell or tissue comprising (a) transplanting the cell or tissue into the subject, wherein the cell or tissue is

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surrounded by a semipermeable membrane that is impermeable to immunoglobulins and (b) treating the subject with a prophylactically effective amount of CTLA4 or CTLA4Ig, wherein the cell surrounded by the semipermeable membrane and the CTLA4 or CTLA4Ig have a synergistic effect so as to inhibit the destruction of the transplanted cell or tissue by the subject's immune system.

**Rejection under 35 U.S.C. §112, First Paragraph**

The Examiner rejected claims 54-59 and 62-69 under 35 U.S.C. §112, first paragraph, as allegedly not enabled for a method of transplanting a viable xenogeneic cell or tissue, using "a proteinaceous construct" that inhibits an immune system costimulation event and microencapsulation of the transplanted cell or tissue. Specifically, the Examiner alleges that in view of a lack of definition of a "proteinaceous construct" that inhibits an immune system costimulation event and microencapsulation of the cell or tissue, a "proteinaceous construct" encompasses any protein inhibitors of an immune system costimulation event, having any structure, wherein the structure of the inhibitors is not necessarily the same as that of CTLA4 or CTLA4Ig, for which the Examiner conceded the claimed method is enabled. Accordingly, the Examiner alleges that it would be undue experimentation to screen the inhibitors for use in the claimed method.

In response, and without conceding the correctness of the Examiner's rejection, applicants note that claims 54-59 and 62-69 have been canceled. Accordingly, the Examiner's rejection thereof is now moot.

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Applicants also note that new claims 71-81, which correspond to old claims 55-57 and 62-69, respectively, satisfy the requirements of 35 U.S.C. §112, first paragraph, because claim 70, upon which claims 71-81 depend, provides a method that, in relevant part, involves treating a subject with a prophylactically effective amount of CTLA4 or CTLA4Ig. Accordingly, because one skilled in the relevant art would know how to make the CTLA4 and CTLA4Ig, it would not require undue experimentation to practice the claimed method.

#### **Rejection under 35 U.S.C. §103**

The Examiner also rejected claims 54-59 and 62-70 under 35 U.S.C. §103 as allegedly obvious over Lenschow et al., in view of Goosen et al., Soon-Shiong et al., Akalin et al., Linsley et al., Padrid et al. and Steurer et al.

Specifically, the Examiner alleges that one would have been motivated to combine the teachings of Lenschow et al. with Soon-Shiong et al. and Goosen et al. with a reasonable expectation of success because CTLA4Ig treatment, as taught by Lenschow et al., and encapsulation of islets, as taught by Soon-Shiong et al. and Goosen et al. are complementary to each other, i.e. both reduce damage by host immune cells to islets. Accordingly, the Examiner alleges that the combination of both treatments would further enhance the chance of graft survival.

The Examiner further stated on page 4 of the Office Action that "concerning the unexpected results of the claimed method, [a]pplicant argues limitation not the claims." Applicants

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understand the Examiner's statement to mean that the unexpected synergistic effect of the claimed method, upon which applicants' earlier assertion of non-obviousness was in part based, was not recited in the claims and was therefore not a claim limitation. Applicants note that the amended claims do recite the term "synergistic effect" as discussed in more detail below.

In response to the Examiner's rejection, applicants respectfully traverse.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim. First, the cited references, when combined, must teach or suggest every limitation of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Applicants maintain that Lenschow et al., in view of Goosen et al., Soon-Shiong et al., Akalin et al., Linsley et al., Padrid et al., and Steurer et al., fail to teach or suggest every limitation of the claims.

Specifically, applicants note that nowhere do the cited references, when combined, teach or suggest a method for transplanting into a subject a viable xenogeneic cell or tissue comprising (a) transplanting the cell or tissue into the subject, wherein the cell or tissue is surrounded by a semipermeable membrane that is impermeable to immunoglobulins and (b) treating the subject with a prophylactically effective amount of CTLA4 or CTLA4Ig, wherein the

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cell surrounded by the semipermeable membrane and the CTLA4 or CTLA4Ig *have a synergistic effect* so as to inhibit the destruction of the transplanted cell or tissue by the subject's immune system.

Applicants note that claim 70, and dependent claims 71-81, reflect their *surprising* discovery which is characterized by a *synergistic* effect on improving transplant survival. That is, the instant method shows improvement in xenogeneic transplant survival rates over survival rates observed with the use of either a semipermeable membrane alone or CTLA4 or CTLA4Ig alone. Accordingly, applicants maintain that the cited references fail to teach or suggest each and every element of the claimed invention. Likewise, applicants assert that there was no reasonable expectation that the claimed method would succeed.

In view of the above remarks, applicants maintain that claims 70-81 satisfy the requirements of 35 U.S.C. §103.

### Summary

In view of the remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

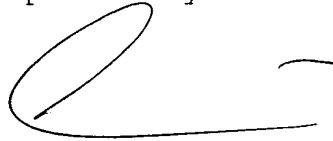
If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this

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Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

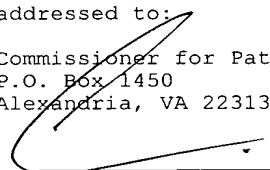
Respectfully submitted,



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2/16/05  
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